Coagulation Guidelines For Unexplained Bleeding Disorders

Washington State Clinical Laboratory Advisory Council
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Washington Department of Laboratory Medicine.

FOR EDUCATIONAL PURPOSES ONLY

The individual clinician is in the best position to determine which tests are most appropriate for a particular patient.

Patient History & Physical Exam Important points to consider in interpreting guidelines: 1) Early onset bleeding (platelets) versus late onset (humoral factor deficiency). 2) Pregnancy (effects on circulatory levels) 3) Hereditary and/or personal history of bleeding disorders- possible (autosomal, recessive, dominant, sex-linked). Basic Coagulation Workup (BCW): aPTT, PT, TT, Fibrinogen, Platelet count Fibrinogen-PT- Normal PT- Prolonged PT- Prolonged Normal Platelet -TT- Prolonged I ow aPTT- Prolonged aPTT- Normal aPTT- Prolonged Coagulation Decreased Platelet- Low TT - Normal Workup Bleeding Other Tests -Normal Patient aPTT 1:1 Mix Add protamin FVII Deficiency. D-Dimer Common Pathway sulfate Liver Disease. Deficiency Vitamin K Possible Causes Complete No or Workup for Deficiency Correction Full ·FX. FII (ex: incomplete after 60 No Isolated Pos Neg a) Mild FVIII Correction Warfarin RX. minutes correction Correction Thrombob) VWD type II a/ Vit K deficiency) (slow (immediate cytopenia II b (autosomal FVX II (ex: liver acting inhibitor) Antibody dominant) disease) Heparin inhibition) Dvsfibragainst c) FX III (autocontamination DIC inogen bovine somal thrombin/ recessive) Do Lupus Do dysfibrinogen d) Fibrinolytic Deficiency of: anti-Factor ·F VIII (hemophilia work-up: coagulant VIII -PAI-1 A, Type I VWD), workup Inhibitor F IX (hemophilia deficiency Fibrin Split (contact workup ·TPA excess B), Products reference. -Alpha 2 ·F XI lab) antiplasmin ·F XII (Hageman deficiency Factor deficiency, No bleeding) Abbreviations: aPTT: Activated Partial Thromboplastin Time DIC: Dessiminated Intravascular Coagulation NOTE: Bleeding time maybe useful as an additional diagnostic tool for familial or F: Factor acquired platelet disorders such as Von Hildebrand's disease or Ticlipod PAI: Plasminogen Activator Inhibitor medication. In general, it is not a predictor of bleeding for surgical procedures. PT: Prothrombin Time TPA: Tissue Plasminogen Activator REFERENCES: Work up extracted from literature and modified by University of VWD: Von Willebrand's Disease

Hypercoagulable State Practice Guidelines

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Definition: Hypercoagulable state: balance of the coagulation system is tipped toward thrombosis, due to either acquired or inherited increase in pro-coagulant elements (e.g. cancer pro coagulant) or decrease in anti-coagulant elements (e.g. Protein C deficiency).

Hypercoaguable states are suspected in patients who have:

- 1)" Spontaneous" thrombosis without obvious associated
- 2) Thrombosis. Even with a concomitant risk factor, at an early age (e.g. less than 40)
- 3) Recurrent thrombosis, especially in different sites

- 4) Strong family history of thrombosis, MI or stroke in young relatives
- 5) Thrombosis in unusual locations (visceral thrombosis, arterial thrombosis in young person)

Acquired Disorders and applicable laboratory test

Initial testing for all patients: PT, PTT, TT, Platelet, Fibrinogen (Refer to Coagulation Guideline for Unexplained Bleeding Disorders on the reverse side)

1) Antiphospholipid antibody (aPL) Syndrome (Lupus anticoagulant)

Test: Anticardiolipin antibodies (ACA titers)

Russell venom time (dRVVT) or platelet neutralization

2) Hyperhomocysteinemia (vitamin deficiency)

Test: Serum Homocysteine

3) Dysfibrinogenemia (liver disease)

Test: Fibrinogen, Thrombin Time, Reptilase Clotting Time

4) Heparin-induced thrombocytopenia

Test: Heparin Antibody

5) Cancer

Test: Use what is general practice for CA diagnosis

Inherited Disorders and applicable laboratory test

Initial testing for all patients: PT, PTT, TT, Platelet, Fibrinogen
(Refer to Coagulation Guideline for Unexplained Bleeding Disorders on the reverse side)

1) Factor V Leiden/aPC resistance (most common)

Test: aPC (activated Protein C) resistance assay - general screen; most common reason for resistance (95%) is factor V Leiden (genetic defect in factor V) **OR** DNA analysis for factor V Leiden - determines if patient is heterozygote or homozygote

 Factor II (Prothrombin G20210) A Deficiency Test: Factor II DNA Analysis

Protein C Deficiency, Protein S Deficiency, Antithrombin III Deficiency
Test together with: Protein C activity, Protein S total and free antigen assays,
Antithrombin activity assay

4) Hyperhomocysteinemia (metabolic defect)

Test: Homocysteine

Dysfibrinogenemia/Fibrinolytic defects
 Test: Fibrinogen, Thrombin, Reptilase Clotting Time

Notes:

At time of acute thrombosis:

- 1) Protein C, Protein S, antithrombin may be falsely low due to consumption in clotting process
- 2) May get reactive (not causative) antiphospholipid antibodies
- 3) Some believe homocysteine is a acute-phase reactant

When on heparin/ coumadin:

- 1) Antithrombin is decreased to 40-60% (hep) (used as cofactor for heparin) and 10-20% (Coumadin)
- 2) Protein C and S may be falsely elevated by 10-20%(hep); 10-20% decreased (Coumadin)
- 3) Functional tests for antiphospholipid antibody may be affected by either.

References:

- Thrombosis with a Possible Hypercoagulable State, K.Hassell MD UCHSC, Denver Co. 2001
- Algorthm for Laboratory Investigation of Hypercoagulable State , RLA Overland Park, KS
- CAP Consensus Conference XXXVI, Diagnosis Issues in Thrombophilia, Nov. 2001

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